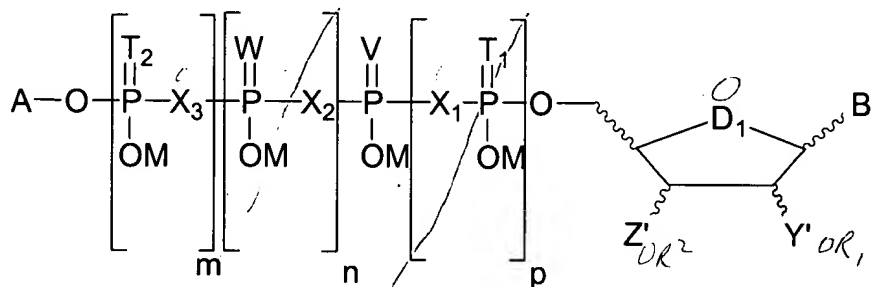


In the Claims

1. (Original) A method of preventing or treating diseases or conditions associated with platelet aggregation comprising:
administering to a subject a pharmaceutical composition comprising a therapeutic effective amount of P2Y₁₂ receptor antagonist compound, wherein said amount is effective to bind P2Y₁₂ receptors on platelets and inhibit ADP-induced platelet aggregation.
2. (Withdrawn)
3. (Currently Amended) The method according to Claim 1, wherein said P2Y₁₂ receptor antagonist compound is a dinucleotide compound of Formula I:

Formula I



wherein:

X₁, X₂, and X₃ are independently oxygen, methylene, monochloromethylene, dichloromethylene, monofluoromethylene, difluoromethylene, or imido;

T₁, T₂, W, and V are independently oxygen or sulfur;

m = 0, 1 or 2;

n = 0 or 1;

p = 0, 1, or 2 ;

where the sum of m+n+p is from 1 to 5;

M = H or a pharmaceutically-acceptable inorganic or organic counterion;

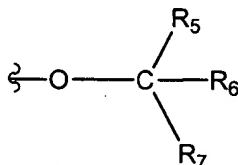
D₁ = O or C;

Y' = H, OH, or OR₁;

Z' = H, OH, or OR₂; with the proviso that at least one of Y' and Z' is OR₁ or OR₂;

R₁ and R₂ are residues which are linked directly to the 2' and /or 3' hydroxyls of the furanose or carbocycle via a carbon atom according to Formula II, or linked directly to two of the 2' and 3' hydroxyls of the furanose or carbocycle via a common carbon atom according to Formula III,

Formula II



wherein:

O is the corresponding 2' and/or 3' oxygen of the furanose or carbocycle;

C is the carbon atom;

R₅, R₆, and R₇ are H, an alkyl, cycloalkyl, aralkyl, aryl, substituted aralkyl, or substituted aryl, such that the moiety defined according to Formula II is an ether; or

R₅ and R₆ are H, an alkyl, cycloalkyl, aralkyl, aryl, substituted aralkyl, or substituted aryl, and R₇ is alkoxy, cycloalkoxy, aralkyloxy, aryloxy, substituted aralkyloxy, or substituted aryloxy such that the moiety defined according to formula II is an acyclic acetal or ketal; or

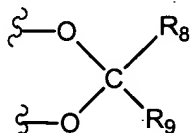
R₅ and R₆ are taken together as oxygen or sulfur doubly bonded to C, and R₇ is alkyl, cycloalkyl, aralkyl, aryl, substituted aralkyl, or substituted aryl, such that the moiety defined according to Formula II is an ester or thioester; or

R₅ and R₆ are taken together as oxygen or sulfur doubly bonded to C, and R₇ is amino or mono- or disubstituted amino, where the substituents are alkyl, cycloalkyl, aralkyl, aryl, substituted aralkyl, or substituted aryl, such that the moiety according to Formula II is a carbamate or thiocarbamate; or

R₅ and R₆ are taken together to mean oxygen or sulfur doubly bonded to C, and R₇ is alkoxy, cycloalkoxy, aralkyloxy, aryloxy, substituted aralkyloxy, or substituted aryloxy, such that the moiety according to Formula II is a carbonate or thiocarbonate; or

R₇ is not present and R₅ and R₆ are taken together as oxygen or sulfur doubly bonded to C and both the 2' and 3' oxygens of the furanose are directly bound to C to form a cyclical carbonate or thiocarbonate;

Formula III



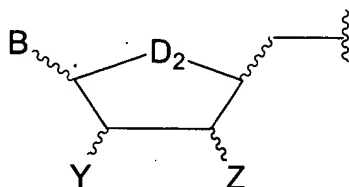
wherein:

O is the 2' and 3' oxygens of the furanose or carbocycle; and the 2' and 3' oxygens of the furanose or carbocycle are linked by the common carbon atom (C) to form a cyclical acetal, cyclical ketal, or cyclical orthoester; and

for cyclical acetals and ketals, R₈ and R₉ are independently hydrogen, alkyl, cycloalkyl, aralkyl, aryl, substituted aralkyl, substituted aryl, or may be joined together to form a homocyclic or heterocyclic ring composed of 3 to 8 atoms, or

for cyclical orthoesters, R₈ is hydrogen, alkyl, cycloalkyl, aralkyl, aryl, substituted aralkyl, or substituted aryl, ~~R₉~~ R₉ is alkyloxy, cycloalkyloxy, aralkyloxy, aryloxy, substituted aralkyloxy, or substituted aryloxy;

A is a nucleoside residue defined as:



and linked to the phosphate chain via the 5' position of the furanose or carbocycle;

wherein:

D₂=O or C;

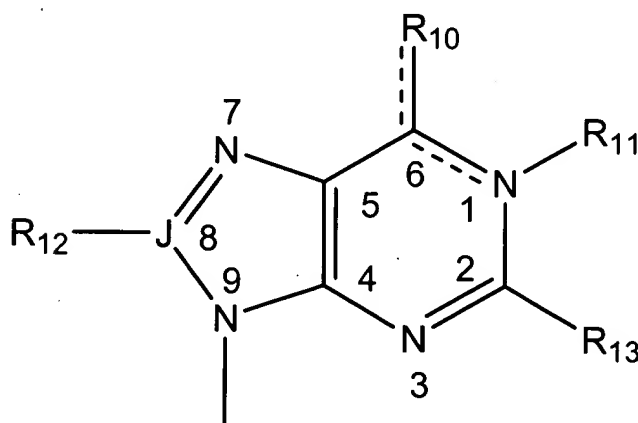
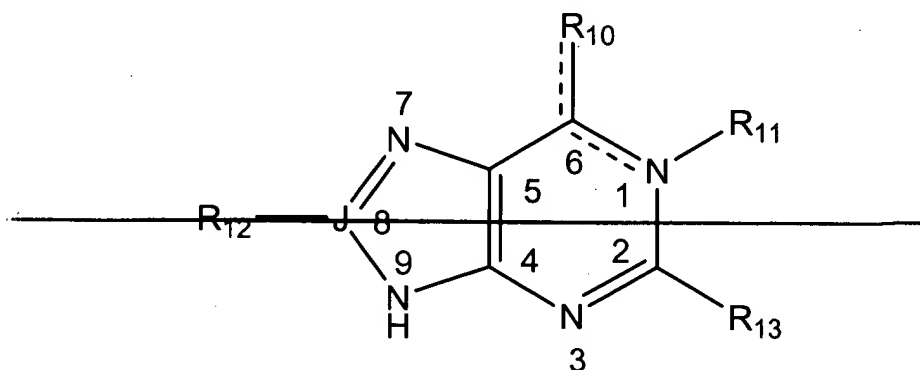
Z =H, OH, or OR₃;

Y =H, OH, or OR₄;

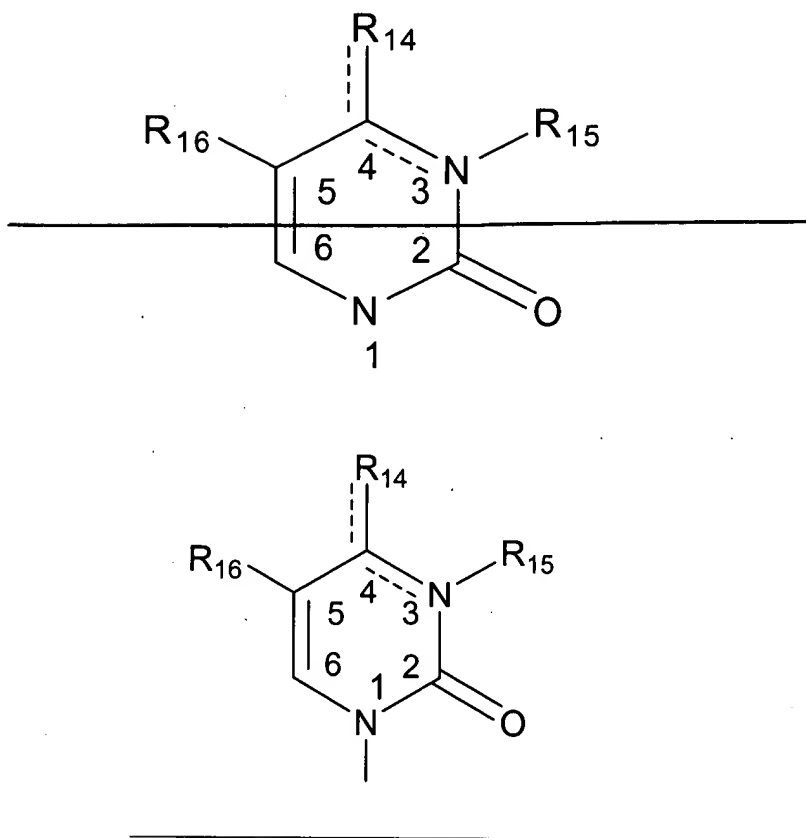
R and R₄ are residues which are linked directly to the 2' and /or 3' hydroxyls of the furanose or carbocycle via a carbon atom according to Formula II, or linked directly to two of the 2' and 3' hydroxyls of the furanose or carbocycle via the common carbon atom according to Formula III;

B' is a purine or a pyrimidine residue according to general Formulae IV and V which is linked to the 1' position of the furanose or carbocycle via the 9- or 1- position of the base, respectively;

Formula IV



Formula V



wherein:

Ad
R₁₀ and R₁₄ are hydroxy, oxo, amino, mercapto, alkylthio, alkyloxy, aryloxy, alkylamino, cycloalkylamino, aralkylamino, arylamino, diaralkylamino, diarylamino, or dialkylamino, where the alkyl groups are optionally linked to form a heterocycle; or

R₁₀ and R₁₄ are acylamino, provided that they incorporate an amino residue from the C-6 position of the purine or the C-4 position of the pyrimidine; or

when R₁₀ in a purine or R₁₄ in a pyrimidine has as its first atom nitrogen, R₁₀ and R₁₁ or R₁₄ and R₁₅ are taken together to form a 5-membered fused imidazole ring (etheno compounds), optionally substituted on the etheno ring with alkyl, cycloalkyl, aralkyl, or aryl moieties, as described for R₅-R₉ above;

J is carbon or nitrogen, with the provision that when nitrogen, R₁₂ is not present;

R₁₁ is hydrogen, O, or is absent;

R₁₅ is hydrogen, or acyl;

R₁₂ is hydrogen, alkyl, azido, alkylamino, arylamino or aralkylamino, alkoxy, aryloxy or aralkyloxy, alkylthio, arylthio or aralkylthio, or ω -A(C₁₋₆alkyl)B-, wherein A and B are independently amino, mercapto, hydroxy or carboxyl; and

R₁₃ is hydrogen, chlorine, amino, monosubstituted amino, disubstituted amino, alkylthio, arylthio, or aralkylthio, where the substituent on sulfur contains up to a maximum of 20 carbon atoms, with or without unsaturation; and

R₁₆ is hydrogen, methyl, alkyl, halo, alkyl, alkenyl, substituted alkenyl, alkynyl, or substituted alkynyl.

4. (Original) The method according to Claim 1, wherein said pharmaceutical composition reduces the incidence of dose-related adverse side effects of other therapeutic agents that are used to prevent, manage or treat platelet aggregation disorders.

Q4 5. (Currently Amended) The method according to Claim 1, wherein said diseases or conditions associated with platelet aggregation are disorders or procedures characterized by thrombosis, primary arterial thrombotic complications of atherosclerotic disease, thrombotic complications of interventions of atherosclerotic disease, thrombotic complications of surgical or mechanical damage, mechanically-induced platelet activation, shunt occlusion, thrombosis secondary to vascular damage and inflammation, indications with a diffuse thrombotic/platelet consumption component, venous thrombosis, coronary arterial thrombosis, pathological effects of atherosclerosis and arteriosclerosis, platelet aggregation and clot formation in blood and blood products during storage, chronic or acute states of hyper-aggregability, reocclusion of an artery or vein following fibrinolytic therapy, platelet adhesion associated with extracorporeal ~~circulation~~, circulation, thrombotic complications associated with thrombolytic therapy, thrombotic complications associated with coronary and other angioplasty, or thrombotic complications associated with coronary artery bypass procedures.

6. (Original) The method according to Claim 5, wherein said disorders or procedures associated with thrombosis are unstable angina, coronary angioplasty, and myocardial infarction;

said primary arterial thrombotic complications of atherosclerosis are thrombotic stroke, peripheral vascular disease, and myocardial infarction without thrombolysis; said thrombotic complications of interventions of atherosclerotic disease are angioplasty, endarterectomy, stent placement, coronary and other vascular graft surgery; said thrombotic complications of surgical or mechanical damage are tissue salvage following surgical or accidental trauma, reconstructive surgery including skin flaps, and "reductive" surgery such as breast reduction; said mechanically – induced platelet activation is caused by cardiopulmonary bypass resulting in microthromboembolism and storage of blood products; said shunt occlusion is renal dialysis and plasmapheresis; said thromboses secondary to vascular damage and inflammation are vasculitis, arteritis, glomerulonephritis and organ graft rejection; said indications with a diffuse thrombotic/platelet consumption component are disseminated intravascular coagulation, thrombotic thrombocytopenic purpura, hemolytic uremic syndrome, heparin-induced thrombocytopenia, and pre-eclampsia/eclampsia; said venous thrombosis are deep vein thrombosis, veno-occlusive disease, hematological conditions, and migraine; and said coronary arterial thrombosis is associated with unstable angina, coronary angioplasty and acute myocardial infarction.

24 7. (Original) The method according to Claim 6, wherein said hematological conditions are thrombocythemia and polycythemia.

8. (Original) The method according to Claim 7, wherein said pathological effects of atherosclerosis and arteriosclerosis are arteriosclerosis, acute myocardial infarction, chronic stable angina, unstable angina, transient ischemic attacks, and strokes, peripheral vascular disease, arterial thrombosis, preeclampsia, embolism, restenosis or abrupt closure following angioplasty, carotid endarterectomy, and anastomosis of vascular grafts; said chronic or acute states of hyper-aggregability is caused by DIC, septicemia, surgical or infectious shock, post-operative and post-partum trauma, cardiopulmonary bypass surgery, incompatible blood transfusion, abruptio placenta, thrombotic thrombocytopenic purpura, snake venom and immune diseases; and said reocclusion of an artery or vein following fibrinolytic therapy is inhibited by internal administration of said compound with a fibrinolytic agent.

9. (Original) The method according to Claim 8, wherein said fibrinolytic agent is a natural or synthetic product which directly or indirectly causes lysis of a fibrin clot.
10. (Original) The method according to Claim 8, wherein said fibrinolytic agent is a plasminogen activator selected from the group consisting of anistreplase, urokinase, pro-urokinase, streptokinase, tissue plasminogen activator and mutants, or variants thereof, which retain plasminogen activator activity.
11. (Original) The method according to Claim 10, wherein said variants are selected from the group consisting of variants which have been chemically modified, variants which one or more amino acids have been added, deleted or substituted, and variants with one or more modified functional domains.
12. (Original) The method according to Claim 11, wherein said modified functional domains are added, deleted or altered by combining the active site of one plasminogen activator or fibrin binding domain of another plasminogen activator or fibrin binding molecule.
13. (Original) The method according to Claim 1, wherein said administering is systemic administration of said compound to a subject.
14. (Original) The method according to Claim 13, wherein said systemic administration is an administration selected from the group consisting of: injecting an injectable form of said compound; administering by mouth an oral form of said compound; applying to the skin a transdermal patch or a transdermal pad containing said compound; administering a liquid/liquid suspension of said compound via nose drops or nasal spray; administering a nebulized liquid of said compound to oral or nasopharyngeal airways; administering rectally a suppository form of said compound; administering vaginally said compound in dosage unit formulations containing conventional non-toxic pharmaceutically acceptable carriers, adjuvants and vehicles; administering said compound intravitreally; and administering via intra-operative instillation a